Amendments to the Specification:

Please delete the paragraph at page 63, line 17 (first full paragraph) and replace it with the following paragraph:

HYB 165, a 18-mer mixed backbone oligonucleotides (MBO) targeted against the N-terminal 8-13 codons of the human RIα regulatory subunit of PKA, synthesized by the procedure previously described was provided by Hybridon Inc., Cambridge, MA. The antisense used had the following sequence: HYB 165, ***GCGU***GCCTCCTCAC***UGGC*** **(SEQ ID NO:4)** and contains 2-O-methyl-modified ribonucleotide bases (bold italics) at the 5' and 3' ends and unmodified oligodeoxynucleotide bases in the middle. Docetaxel was a kind gift from Rhone Poulenc Rorer, Origgio, Italy, and used after dilution in appropriate solvent as 100x concentrated stock. The monoclonal antibody MAb C225 is a human-mouse chimeric IgG_1 that binds to the EGFR, competes with natural ligands for receptor binding and blocks the EGFR tyrosine kinase activation. Clinical grade MAb C225 was kindly provided by Dr. H. Waksal, ImClone Systems, New York, NY.

Please delete the paragraph at page 65, line 18 (first full paragraph) and replace it with the following paragraph:

HYB 508, a 18-mer mixed backbone oligonucleotides (MBO) targeted against the N-terminal 8-13 codons of the human RIα regulatory subunit of PKA, synthesized by the procedure previously described was provided by Hybridon Inc., Cambridge, MA. The antisense used had the following sequence: HYB 508, ***GCAU***GCTTCCACAC**AGGC** **(SEQ ID NO:9)** and contains 2-O-methyl-modified ribonucleotide bases (bold italics) at the 5' and 3' ends and unmodified oligodeoxynucleotide bases in the middle. HYB 508 is a control oligonucleotide of HYB 165, containing four mismatched nucleotides (underlined). Docetaxel was a kind gift from Rhone Poulenc Rorer, Origgio, Italy, and used after dilution in appropriate solvent as 100x concentrated stock. The monoclonal antibody MAb C225 is a human-mouse chimeric IgG_1 that binds to the EGFR, competes with natural ligands for receptor binding and blocks the EGFR tyrosine kinase activation. Clinical grade MAb C225 was kindly provided by Dr. H. Waksal, ImClone Systems, New York, NY.

Please delete the paragraph at page 67, line 16 (first full paragraph) and replace it with the following paragraph:

HYB 165, a 18-mer mixed backbone oligonucleotides (MBO) targeted against the N-terminal 8-13 codons of the human RI_α regulatory subunit of PKA, synthesized by the procedure previously described was provided by Hybridon Inc., Cambridge, MA. The antisense used had the following sequence: HYB 165, ***GCGU***GCCTCCTCAC***UGGC*** **(SEQ ID NO:4)** and contains 2-O-methyl-modified ribonucleotide bases (bold italics) at the 5' and 3' ends and unmodified oligodeoxynucleotide bases in the middle. Paclitaxel was purchased from Sigma (St Louis, MO) and used after dilution in appropriate solvent as 100x concentrated stock.

Please delete the paragraph at page 69, line 13 (first full paragraph) and replace it with the following paragraph:

Materials. 18-mer mixed backbone oligonucleotides (MBO) targeted against the N-terminal 8-13 codons of the human RIα regulatory subunit of PKA, synthesized by the procedure previously described were provided by Hybridon Inc., Cambridge, MA. The antisense used had the following sequences: HYB 165, ***GCGU***GCCTCCTCAC***UGGC*** **(SEQ ID NO:4)**; HYB 508, ***GCAU***GCTTCCACAC**AGGC** **(SEQ ID NO:9)**. HYB 165 and HYB 508 are chimeric compounds containing 2-O-methyl-modified ribonucleotide bases (bold italics) at the 5' and 3' ends and unmodified oligodeoxynucleotide bases in the middle. HYB 508 is a control oligo containing four mismatched nucleotides as underlined.

Please delete the paragraph at page 71, line 13 (first full paragraph) and replace it with the following paragraph:

Materials. 18-mer mixed backbone oligonucleotides (MBO) targeted against the N-terminal 8-13 codons of the human RIα regulatory subunit of PKA, synthesized by the procedure previously described were provided by Hybridon Inc., Cambridge, MA. The antisense used had the following sequences: HYB 165, ***GCGU***GCCTCCTCAC***UGGC*** **(SEQ ID NO:4)**; HYB 508, ***GCAU***GCTTCCACAC***AGGC*** **(SEQ ID NO:9)**. HYB 165 and HYB 508 are chimeric compounds containing 2-O-methyl-modified ribonucleotide bases (bold italics) at the 5' and 3' ends and unmodified oligodeoxynucleotide bases in the middle. HYB 508 is a control oligo containing four mismatched nucleotides as underlined.

Please delete the paragraph at page 73, line 13 (first full paragraph) and replace it with the following paragraph:

Materials. 18-mer mixed backbone oligonucleotides (MBO) targeted against the N-terminal 8-13 codons of the human RIα regulatory subunit of PKA, synthesized by the procedure previously described were provided by Hybridon Inc., Cambridge, MA. The antisense used had the following sequences: HYB 165, ***GCGU***GCCTCCTCAC***UGGC*** **(SEQ ID NO:4)**; HYB 508, ***GCAU***GCTTCCACAC***AGGC*** **(SEQ ID NO:9)**. HYB 165 and HYB 508 are chimeric compounds containing 2-O-methyl-modified ribonucleotide bases (bold italics) at the 5' and 3' ends and unmodified oligodeoxynucleotide bases in the middle. HYB 508 is a control oligo containing four mismatched nucleotides as underlined.

Please delete the paragraph at page 75, line 8 (title) and replace it with the following paragraph:

EFFECT OF HYB 508 WITH OR WITHOUT MONOCLONAL ANTIBODY [[Mab]]MAb C225 ON THE GROWTH OF ZR-75-1 HUMAN BREAST CANCER CELLS

Please delete the paragraph at page 75, line 14 (first full paragraph) and replace it with the following paragraphs:

Materials. HYB 508, a 18-mer mixed backbone oligonucleotides (MBO) targeted against the N-terminal 8-13 codons of the human RIα regulatory subunit of PKA, synthesized by the procedure previously described was provided by Hybridon Inc., Cambridge, MA. The antisense used had the following sequence: HYB 508, ***GCAUGCTTCCACACAGGC*** **(SEQ ID NO:9)** and contains 2-O-methyl-modified ribonucleotide bases (bold italics) at the 5' and 3' ends and unmodified oligodeoxynucleotide bases in the middle. HYB 508 is a control oligonucleotide of HYB 165, containing four mismatched nucleotides (underlined). The monoclonal antibody [[Mab]]**MAb** C225 is a human-mouse chimeric IgG_1 that binds to the EGFR, competes with natural ligands for receptor binding and blocks the EGFR tyrosine kinase activation. Clinical grade MAbC225 was- kindly provided by Dr. H. Waksal, ImClone Systems, New York, NY.

Cell lines. ZR-75-1 human breast cancer cells were purchased from American Type Culture Collection (Rockville, MD, USA). Cells were maintained in DMEM medium supplemented with 10% heat-inactivated FBS, 20 mM HEPES, pH 7.4, penicillin (100 UI/ml), streptomycin (100 µg/ml) and 4 mM glutamine (ICN, Irvine, UK) in a humified atmosphere of 95% air and 5% CO_2 at 37° C.

Please delete the paragraph at page 75, line 30 (second full paragraph) and replace it with the following paragraphs:

Soft agar growth. Cells (10^4 cells/well) were seeded in 0.5 ml of 0.3% Difco Noble agar (Difco, Detroit, MI) supplemented with complete culture medium. This suspension was layered over 0.5 ml of 0.8% agar-medium base layer in 24 multiwell cluster dishes (Becton Dickinson) and treated with various concentrations of [[Mab]]**MAb** C225 and/or of HYB 508 every 48 hours for three times. After 12 days the cells were stained with nitroblue tetrazolium (Sigma) and colonies larger than 0.05 mm were counted.

Experiments were performed twice in triplicate.

Please delete the paragraph at page 76, line 2 (first full paragraph) and replace it with the following paragraph:

HYB 508 0.5 µM (i-l), which alone causes about 5% inhibition of ZR-75-1 cell growth, was used in combination with *i*) [[Mab]]**MAb** C225 0.25 µg/ml, which alone causes about 10% inhibition, determining an average 12% inhibition; *j*) [[Mab]]**MAb** C225 0.5 µg/ml, which alone causes about 47% inhibition, determining an average 45% inhibition; *k*) [[Mab]]**MAb** C225 1 µg/ml, which alone causes about 68% inhibition, determining an average 77% inhibition; *l*) [[Mab]]**MAb** C225 2.5 µg/ml, which alone causes about 76% inhibition, determining an average 82% inhibition. See Figure 8.

Please delete the paragraph at page 76, line 10 (second full paragraph) and replace it with the following paragraph:

HYB 508 at the dose of 0.5 μM showed no cooperative antiproliferative effect on the growth of ZR-75-1 cells when used in combination with different doses of [[Mab]]**MAb** C225.

Please delete the paragraph at page 77, line 13 (first full paragraph) and replace it with the following paragraph:

Materials. 18-mer mixed backbone oligonucleotides (MBO) targeted against the N-terminal 8-13 codons of the human RIα regulatory subunit of PKA, synthesized by the procedure previously described were provided by Hybridon Inc., Cambridge, MA. The antisense used had the following sequences: HYB 165, ***GCGU***GCCTCCTCAC***UGGC*** **(SEQ ID NO:4)**; HYB 618, ***GCAU***GCATCCGCAC***AGGC*** **(SEQ ID NO:10)**. HYB 165 and HYB 618 are chimeric compounds containing 2-O-methyl-modified ribonucleotide bases (bold italics) at the 5' and 3' ends and unmodified oligodeoxynucleotide bases in the middle. HYB 618 is a control oligo containing four mismatched nucleotides as underlined.

Please delete the paragraph at page 79, line 16 (first full paragraph) and replace it with the following paragraph:

Materials. HYB 165, a 18-mer mixed backbone oligonucleotides (MBO) targeted against the N-terminal 8-13 codons of the human RIα regulatory subunit of PKA, synthesized by the procedure previously described was provided by Hybridon Inc., Cambridge, MA. The antisense used had the following sequence: HYB 165, ***GCGU***GCCTCCTCAC***UGGC*** **(SEQ ID NO:4)** and contains 2-O-methyl-modified ribonucleotide bases (bold italics) at the 5' and 3' ends and unmodified oligodeoxynucleotide bases in the middle. Docetaxel was a kind gift from Rhone Poulenc Rorer, Origgio, Italy, and used after dilution in appropriate solvent as 100x concentrated stock.

Please delete the paragraph at page 81, line 16 (first full paragraph) and replace it with the following paragraph:

Materials. HYB 508, a 18-mer mixed backbone oligonucleotides (MBO) targeted against the N-terminal 8-13 codons of the human RIα regulatory subunit of PKA, synthesized by the procedure previously described was provided by Hybridon Inc., Cambridge, MA. The antisense used had the following sequence: HYB 508, ***GCAU***GCTTCCACAC***AGGC*** **(SEQ ID NO:9)** and contains 2-O-methyl-modified ribonucleotide bases (bold italics) at the 5' and 3' ends and unmodified oligodeoxynucleotide bases in the middle. HYB 508 is a control oligonucleotide of HYB 165, containing four mismatched nucleotides (underlined). Docetaxel was a kind gift from Rhone Poulenc Rorer, Origgio, Italy, and used after dilution in appropriate solvent as 100x concentrated stock.

Please delete the paragraph at page 83, line 14 (first full paragraph) and replace it with the following paragraphs:

Materials. HYB 165, a 18-mer mixed backbone oligonucleotides (MBO) targeted against the N-terminal 8-13 codons of the human RIα regulatory subunit of PKA, synthesized by the procedure previously described was provided by Hybridon Inc., Cambridge, MA. The antisense used had the following sequence: HYB 165, ***GCGU***GCCTCCTCAC***UGGC*** **(SEQ ID NO:4)**, and contains 2-O-methyl-modified ribonucleotide bases (bold italics) at the 5' and 3' ends and unmodified oligodeoxynucleotide bases in the middle. The monoclonal antibody MAb C225 is a human-mouse chimeric IgG_1 that binds to the EGFR, competes with natural ligands for receptor binding and blocks the EGFR tyrosine kinase activation. Clinical grade MAb C225 was kindly provided by Dr. H. Waksal, ImClone Systems, New York, NY.

Cell lines. ZR-75-1 human breast cancer cells were purchased from American Type Culture Collection (Rockville, MD, USA). Cells were maintained in DMEM medium supplemented with 10% heat-inactivated FBS, 20 mM HEPES, pH 7.4 penicillin (100 UI/ml), streptomycin (100 µg/ml) and 4 mM glutamine (ICN, Irvine, UK) in a humified atmosphere of 95% air and 5% CO_2 at 37° C.

Please delete the paragraph at page 83, line 29 (second full paragraph) and replace it with the following paragraphs:

Soft agar growth. Cells (10^4 cells/well) were seeded in 0.5 ml of 0.3% Difco Noble agar (Difco, Detroit, MI) supplemented with complete culture medium. This suspension was layered over 0.5 ml of 0.8% agar-medium base layer in 24 multiwell cluster dishes (Becton Dickinson) and treated with various concentrations of [[Mab]]**MAb** C225 and/or of HYB 165 every 48 hours for three times. After 12 days the cells were stained with nitroblue tetrazolium (Sigma) and colonies larger than 0.05 mm were counted.

Experiments were performed twice in triplicate.

Please delete the paragraph at page 84, line 2 (first full paragraph) and replace it with the following paragraphs:

HYB 165 0.1 µM (a-d), which alone causes about 2% inhibition of ZR-75-1 cell growth, was used in combination with *a*) [[Mab]]**MAb** C225 0.25 µg/ml, which alone causes about 10% inhibition, determining an average 37% inhibition; *b*) [[Mab]]**MAb** C225 0.5 µg/ml, which alone causes about 47% inhibition, determining an average 65% inhibition; *c*) [[Mab]]**MAb** C225 1 µg/ml, which alone causes about 68% inhibition, determining an average 85% inhibition; *d*) [[Mab]]**MAb** C225 2.5 µg/ml, which alone causes about 76% inhibition, determining an average 90% inhibition.

HYB 165 at the higher dose of 0.5 µM (e-h), which alone causes about 10% inhibition of ZR-75-1 cell growth, was used in combination with *e*) [[Mab]]**MAb** C225 0.25 µg/ml, which alone

causes about 10% inhibition, determining an average 57% inhibition; *f*) [[Mab]]**MAb** C225 0.5 μg/ml, which alone causes about 47% inhibition, determining an average 70% inhibition; *g*) [[Mab]]**MAb** C225 1 μg/ml, which alone causes about 68% inhibition, determining an average 90% inhibition; *h*) [[Mab]]**MAb** C225 2.5 μg/ml, which alone causes about 76% inhibition, determining an average 98% inhibition. See Figure 12.

Please delete the paragraph at page 84, line 16 (second full paragraph) and replace it with the following paragraph:

HYB 165 at the low inhibitory dose of 0.1 μM and 0.5 μM cooperatively inhibit the growth of ZR-75-1 cells when used in combination with different doses of [[Mab]]**MAb** C225.

Please delete the paragraph at page 85, line 14 (first full paragraph) and replace it with the following paragraph:

Materials. 18-mer mixed backbone oligonucleotides (MBO) targeted against the N-terminal 8-13 codons of the human RIα regulatory subunit of PKA, synthesized by the procedure previously described were provided by Hybridon Inc., Cambridge, MA. The antisense used had the following sequences: HYB 165, ***GCGU***GCCTCCTCAC***UGGC*** **(SEQ ID NO:4)**; HYB 295, ***GCAU***GCATCCGCAC***AGGC*** **(SEQ ID NO:10)**. HYB 165 and HYB 295 are chimeric compounds containing 2-O-methyl-modified ribonucleotide bases (bold italics) at the 5' and 3' ends and unmodified oligodeoxynucleotide bases in the middle. HYB 295 is a control oligo containing four mismatched nucleotides as underlined.

Please delete the paragraph at page 87, line 14 (first full paragraph) and replace it with the following paragraph:

18-mer mixed backbone oligonucleotides (MBO) targeted against the N-terminal 8-13 codons of the human RIα regulatory subunit of PKA, synthesized by the procedure previously described were provided by Hybridon Inc., Cambridge, MA. The antisense used had the following sequences: HYB 165, ***GCGU***GCCTCCTCAC***UGGC*** **(SEQ ID NO:4)**; HYB 508, ***GCAU***GCTTCCACAC***AGGC*** **(SEQ ID NO:9)**. HYB 165 and HYB 508 are chimeric compounds containing 2-O-methyl-modified ribonucleotide bases (bold italics) at the 5' and 3' ends and unmodified oligodeoxynucleotide bases in the middle. HYB 508 is a control oligo containing four mismatched nucleotides as underlined.

Please delete the paragraph at page 89, line 13 (first full paragraph) and replace it with the following paragraph:

Materials. 18-mer mixed backbone oligonucleotides (MBO), targeted against the N-terminal 8-13 codons of the human RIα regulatory subunit of PKA, synthesized by the procedure previously described were provided by Hybridon Inc., Cambridge, MA. The antisense used had the following sequences: HYB 165, ***GCGU***GCCTCCTCAC***UGGC*** **(SEQ ID NO:4)**; HYB 295,

GCAUGCATCCGCAC***AGGC*** **(SEQ ID NO:10)**. HYB 165 and HYB 295 are chimeric compounds containing 2-O-methyl-modified ribonucleotide bases (bold italics) at the 5' and 3' ends and unmodified oligodeoxynucleotide bases in the middle. HYB 295 is a control oligo containing four mismatched nucleotides as underlined.

Please delete the sequence listing at pages 96-99 and replace it with the new sequence listing provided with this submission.